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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,496	DELOBEL ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-26* is/are pending in the application.

4a) Of the above claim(s) *21-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0502*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on May 14, 2002 is acknowledged. The traversal is on the ground(s) that the subject matter of the present invention is the use of Pa1b protein as an insecticide, which use is not disclosed in the prior art, and which use is the special technical feature shared by the two groups of invention. The traversal is also on the ground(s) that the office has not applied the same unity of invention standard applied by the International Preliminary Examination authority. The traversal is additionally on the ground(s) that the office has not shown that search and examination of all claims would pose a burden. The traversal is further on the ground(s) that the species election requirement is improper, as the recited species share a common significant structural element (Formula I) and a common function (insecticidal activity.

This is not found persuasive because the use of Pa1b protein as an insecticide is not the special technical feature shared by the two groups of invention, as the methods of group II require the use of a polynucleotide, which does not share a common significant structural element and a common function with a polypeptide. This is also not found persuasive because the office has applied the same unity of invention standard applied by the International Preliminary Examination authority, but the office has elected to impose a restriction requirement in view of the lack of unity that exists between the two inventions. This is additionally not found persuasive because the invention of group I requires a search for polypeptides and methods of using polypeptides to treat a plant, whereas the invention of group II requires a search for polynucleotides and methods of

using polynucleotides to make transgenic plants that are insect resistant, such that the search and examination of all the claims would pose an undue burden.

Upon further consideration, the requirement for a species election is withdrawn.

The requirement for restriction between the inventions of groups I and II is still deemed proper and is therefore made FINAL. Accordingly claims 21-26 are withdrawn.

Information Disclosure Statement

An initialed and dated copy of Applicant's IDS form 1449, filed May 14, 2002 is attached to the instant Office action.

Specification

The disclosure is objected to because of the following informalities: the specification lacks a brief description of the drawings. The specification also does not comply with the sequence rules in that reference is made to an amino acid sequence without the use of a sequence identifier. See 37 CFR 1.121 (d), "Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application."

Appropriate correction is required.

Claim Objections

Claim 13 is objected to because of the following informalities: the claim does not comply with the sequence rules in that in that reference is made to an amino acid sequence without the use of a sequence identifier. See 37 CFR 1.121 (d), "Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of protecting a plant from insects comprising treating the plant with a composition comprising a polypeptide having a sequence of the formula $X_1CX_2CX_3CX_4CX_5CX_6CX_7$, wherein C represents a cysteine, and wherein X_1-X_7 represent any undefined amino acid of defined variable intervals, or wherein X_1-X_7

represent defined amino acids of defined intervals, including polypeptides having at least 60% identity with any one of the isoforms of PA1b albumin, and including PA1b albumins and leginsulins.

The specification describes a polypeptide designated "TP" that was purified from pea and that exhibits insecticidal activity (pages 10-14 Example 2). The TP polypeptide is described as consisting of 37 amino acid residues, and having a mass of 3741.1 Da and lacking post-translational modifications (page 13). The TP polypeptide is also described as being strongly homologous to PA1b pea albumin, from which it differs only at amino acid position 29, which is occupied by valine in TP and isoleucine in PA1b (page 13; Figure 7). The TP polypeptide is additionally described as being homologous to soybean leginsulin, with which it shares 62% identity and 89% homology (page 13; Figure 7). The TP polypeptide is further described as comprising six cysteine residues at conserved positions which play an essential role in the structure of the protein (page 14). The specification also describes an undisclosed number of insecticidal polypeptides within the F1 purification fraction as being identical to TP in their first ten N-terminal amino acids and as having masses similar to that of TP (page 14).

The specification does not describe other insecticidal polypeptides that meet the structural limitations of the claims. The specification also does not describe the amino acid sequence of any PA1b albumin isoform, or any insecticidal polypeptide having at least 60% identity with a PA1b isoform. The specification additionally does not describe any additional PA1b albumins or leginsulins other than the PA1b pea albumin and the soybean leginsulin. The specification further does not describe or characterize any PA1b albumin or leginsulin polypeptide as having insecticidal activity.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

In the instant case Applicant has not described a representative number of species falling within the scope of the claimed genus which encompasses a multitude of polypeptides having a sequence of the formula $X_1CX_2CX_3CX_4CX_5CX_6CX_7$, wherein C represents a cysteine, and wherein X_1-X_7 represent any undefined amino acid of defined variable intervals, or wherein X_1-X_7 represent defined amino acids of defined intervals, including polypeptides having at least 60% identity with any one of the isoforms of PA1b albumin, and including PA1b albumins and leginsulins, nor the structural features unique to the genus that are correlated with insecticidal activity.

Claims 13-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of protecting a plant from insects comprising treating the plant with a composition comprising a polypeptide having a sequence of the disclosed TP polypeptide, does not reasonably provide enablement for methods comprising treating the plant with other compositions comprising other polypeptides having other sequences. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of protecting a plant from insects comprising treating the plant with a composition comprising a polypeptide having a sequence of the formula $X_1CX_2CX_3CX_4CX_5CX_6CX_7$, wherein C represents a cysteine, and wherein X_1-X_7 represent any undefined amino acid of defined variable intervals, or wherein X_1-X_7 represent defined amino acids of defined intervals, including polypeptides having at least 60% identity with any one of the isoforms of PA1b albumin, and including PA1b albumins and leginsulins.

The specification discloses the purification from pea of a polypeptide designated "TP" that exhibits insecticidal activity (pages 10-14 Example 2). The TP polypeptide is disclosed as consisting of 37 amino acid residues and as being strongly homologous to PA1b pea albumin, from which it differs only at amino acid position 29, which is occupied by valine in TP and isoleucine in PA1b (page 13; Figure 7). The TP polypeptide is additionally disclosed as being homologous to soybean leginsulin, with which it shares 62% identity and 89% homology (page 13; Figure 7). The TP polypeptide is further disclosed as comprising six cysteine residues at conserved positions which play an essential role in the structure of the protein (page 14). The specification also discloses that the F1 purification fraction comprises an unspecified number of insecticidal polypeptides that are identical to TP in their first ten N-terminal amino acids and that have masses similar to that of TP (page 14).

With respect to the functional properties of the aforementioned polypeptides, the specification that the TP and F1 purification fractions exhibit toxicity to *Sitophilus oryzae*

weevils equivalent to that of pea meal at a concentration of 1% (3 mmol/kg), with a concentration of 60 umol/kg being sufficient to prevent infestation (page 14). The specification also discloses that the TP and F1 purification fractions extracted from dried seed stored for several years conserve their insecticidal activity, and the activity is not affected by heating to 100 C (page 14). The specification additionally discloses the toxicity of the TP protein for the flour moth *Ephestia kuehniella* and the aphid *Acyrthosiphon pisum* (page 15; Figures 8 and 9).

The specification does not disclose other insecticidal polypeptides that meet the structural limitations of the claims. The specification also does not disclose the amino acid sequence of any PA1b albumin isoform, or any insecticidal polypeptide having at least 60% identity with a PA1b isoform. The specification additionally does not disclose any additional PA1b albumins or leginsulins other than the PA1b pea albumin and the soybean leginsulin. The specification further does not disclose or characterize any PA1b albumin or leginsulin polypeptide as having insecticidal activity.

The full scope of the claimed invention is not enabled because it is unpredictable whether the multitude of polypeptide sequences recited in the claims would have insecticidal activity, as changing the number or nature of amino acids in a polypeptide sequence may alter or eliminate the activity of the polypeptide.

See, for example, Chen et al. (Journal of Biological Chemistry, 17 March 1995, Vol. 270, No. 11, pages 6412-6419), who teach that mutations resulting in single amino acid substitutions can attenuate or inactivate the insecticidal toxicity of the *Bacillus thuringiensis* δ-endotoxin. Insecticidal toxicity of the endotoxin was attenuated by the substitution of aspartic acid for tyrosine at residue 153, and was inactivated by the

substitution of glutamic acid for alanine at residue 92. (Abstract page 1 of online reprint, *Effect of Mutations on Toxicity* page 10 of online reprint).

In the instant case Applicant has not provided guidance with respect to the identity and source of polypeptide sequence variants as recited in the claims, or with respect to the specific amino acid structural elements that would be retained by insecticidally active forms of these variants that would further function to protect plants from insects. Absent such guidance it would require undue experimentation for one skilled in the art to identify polypeptide sequence variants that function to protect plants from insects, as one skilled in the art would have to isolate from undisclosed sources and/or synthesize the variant polypeptide sequences, and then test each sequence to determine whether or not it has insecticidal activity and whether or not it would further function to protect plants from insects. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 13, and claims dependent thereon, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 13 is indefinite in the use of parentheses, as it is unclear whether the subject matter enclosed within the parentheses is intended to be a claim limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Iizuka et al. (US Patent No. 5,516,514, issued 14 May 1996) in view of Raikhel (US Patent No. 5,276,269, issued 4 January 1994).

The claim is drawn to a method of protecting a plant from insects comprising treating the plant with a composition comprising a polypeptide having a sequence of the formula $X_1CX_2CX_3CX_4CX_5CX_6CX_7$, wherein C represents a cysteine, and wherein X_1-X_7 represent any undefined amino acid of defined variable intervals.

Iizuka et al. teach a method of protecting a plant from insects comprising treating the plant with a composition comprising a *Bacillus thuringiensis* polypeptide (column 13 claim 4).

Iizuka et al. do not teach treating the plant with a composition comprising a polypeptide having a sequence of the formula $X_1CX_2CX_3CX_4CX_5CX_6CX_7$, wherein C represents a cysteine, and wherein X_1-X_7 represent any undefined amino acid of defined variable intervals.

Raikhel teaches a wheat germ agglutinin isolectin WGA-A polypeptide having a sequence of the formula $X_1CX_2CX_3CX_4CX_5CX_6CX_7$, wherein C represents a cysteine,

and wherein X_1-X_7 represent any undefined amino acid of defined variable intervals, and having insecticidal activity (figure 6 and attached sequence alignment).

Given the success of Iizuka et al. in protecting a plant from insects by treating the plant with a composition comprising a *Bacillus thuringiensis* polypeptide, and given the teaching of Raikhel that the wheat germ agglutinin isolectin WGA-A polypeptide has insecticidal activity, it would have been *prima facie* obvious at the time the invention was made to substitute the wheat germ agglutinin isolectin WGA-A polypeptide taught by Raikhel for the *Bacillus thuringiensis* polypeptide in the method taught by Iizuka et al. One skilled in the art would have been motivated to do so in order to protect a plant from those insects that exhibit sensitivity to the wheat germ agglutinin isolectin WGA-A polypeptide (cowpea weevil). One skilled in the art would have a reasonable expectation of success given the success of Iizuka et al. in protecting a plant from insects by treating the plant with a composition comprising a *Bacillus thuringiensis* polypeptide and given the teaching of Raikhel that the wheat germ agglutinin isolectin WGA-A polypeptide has insecticidal activity.

Remarks

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins Cynthia Collins 9/20/04